Perspectives in Medicine (2012) 1, 228—231

Bartels E, Bartels S, Poppert H (Editors):
New Trends in Neurosonology and Cerebral Hemodynamics — an Update.
Perspectives in Medicine (2012) 1, 228—231

journal homepage: www.elsevier.com/locate/permed

Patent foramen ovale

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KEYWORDS
Patent foramen ovale;
Right-to-left shunt;
Transcranial Doppler sonography;
Ultrasound contrast agent;
Transesophageal echocardiography;
Cryptogenic stroke

Summary Paradoxical embolism is a possible cause of ischemic stroke, particularly in younger patients without any other cause, i.e. cryptogenic stroke, and a patent foramen ovale is the most frequently assumed cause. The contrast transcranial Doppler monitoring mode has a sensitivity that is comparable to contrast transesophageal echocardiography for detection of a right-to-left shunt, however, the contrast transesophageal echocardiography remains the ''golden standard'' for the detection of a patent foramen ovale. Diagnostic studies that can identify a patent foramen ovale may be considered for prognostic purposes. In most cases, however, it is difficult to establish a firm etiological association and the debate about medical or interventional management is ongoing. Other possible causes of right-to-left shunting leading to cerebral complications like pulmonary arteriovenous malformations have also been noted but are rarely discussed.

Introduction

Patients with cryptogenic stroke should be screened for possible paradoxical cerebral embolism via a cardiac or pulmonary right-to-left shunt (RLS).

There is evidence for an increased prevalence of patent foramen ovale (PFO) in cryptogenic stroke, in both younger [1—5] and elderly patients [6]. An atrial septal aneurysm (ASA) may increase the stroke risk as well, whether occurring alone or combined with a PFO [2,5]. Diagnostic studies that can identify PFO with RLS or ASA may be considered for prognostic purposes [7]. Echocardiography is recommended in selected stroke and TIA patients and is particularly required in patients with suspected paradoxical embolism and no other identifiable causes of stroke [8]. Transesophageal echocardiography (TEE) is superior to transthoracic echocardiography for evaluation of the aortic arch, left atrium, and atrial septum [9] and represents the ''golden standard'' to establish the presence of a RLS and a PFO. The contrast transcranial Doppler (cTCD) monitoring mode has a sensitivity that is comparable to contrast TEE (cTEE) for detection of a PFO with RLS. Its diagnostic sensitivity ranges from 70% to 100% and the specificity is more than 95% [10,11].

Although positive cTCD studies in pulmonary RLS have been described, only cTEE allows localization of the RLS to the cardiac or pulmonary level [12—15]. The distinction between cardiac and pulmonary shunts based on the time window of contrast appearance and contrast amount shunted is unreliable by cTCD [13,16].

cTCD allows estimation of the shunt size by quantification and categorization of the contrast shunted. The results are comparable with shunt quantification using cTEE [3,11,17—21]. Large RLS assessed by cTCD have been reported to be associated with a higher risk of first and recurrent stroke, particularly with cryptogenic stroke [17,22]. In contrast, results of a study showed that massive RLS sized with TCD were not an independent risk factor for recurrent stroke [18]. Therefore, the clinical significance of cTCD shunt sizing remains unclear.

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2211-968X
http://dx.doi.org/10.1016/j.permed.2012.03.003

Table 1 Summary of test procedures for detection of right-to-left shunt with ultrasound contrast agent and transcranial Doppler sonography ([16], modified).

Preparation of the patient and TCD recording
Supine position. Insert 18-gauge needle — preferred over a 20-gauge needle to increase the sensitivity [56] — into (right) cubital vein. A higher sensitivity is reported by using the femoral vein as injection site [43] which is, however, more uncomfortable for the patient. Insonate (if possible both) middle cerebral arteries (MCA), bilateral recordings increase the sensitivity compared with unilateral insonation [12,34]. In case of insufficient acoustic bone window, transforaminal insonation of the basilar artery might be an alternative approach [57].
Preparation of contrast agent and injection
Syringe I: 9 ml saline; syringe II: 1 ml air. Connect both syringes with three-way stopcock connected with a short flexible line to an intravenous line of 18-gauge with the patient. Exchange air/saline mixture vigorously between the syringes at least ten times. Inject immediately as a bolus. In case of little or no detection of microembolic signals, repeat the examination with Valsalva maneuver. Commercially traded contrast agents should be prepared according to the manufacturer's instructions.
Application of Valsalva maneuver
The patient should start with Valsalva maneuver on examiner's command 5 s after injection of the contrast agent; the control of an adequate Valsalva maneuver will be performed by assessment of the reduction of peak flow velocity of the TCD curve. Overall Valsalva maneuver duration should be 10 s.
Evaluation of test results
Categorization (for unilateral testing, values for bilateral monitoring in parentheses): (1) 0 microembolic signals (negative result); (2) 1—10 (1—20) microembolic signals; (3) >10 (>20) microembolic signals, but no curtain; (4) curtain or shower of microembolic signals, where a single signal cannot be discriminated within the TCD spectra. The microembolic signal count must be documented and evaluated separately for baseline condition and Valsalva maneuver.

The impact of cTCD in RLS detection has been studied in a number of conditions other than cerebrovascular disease; however, the grade of evidence from these studies is low to moderate: a significant association was reported between the degree of cTCD sized shunting and the number of signal abnormalities on MRI in asymptomatic sport divers [23]. Divers with RLS show a higher risk of decompression sickness [24]. There is evidence of an increased prevalence of PFO in patients with migraine with aura [25], supported by cTCD studies [26,27]. Furthermore, cTCD has been described to be useful to detect residual shunting following transcatheter closure of a PFO [28].

Depending on methodological factors, cTCD results vary considerably. Therefore, criteria of the examination technique were established by an International Consensus Meeting. The goal was a standardized approach and minimal variability for RLS detection by cTCD [16]. The examination technique recommended by this Consensus Meeting is summarized in Table 1.

Fig. 1 shows a video demonstration of a positive contrast study in a patient with large PFO. Additional data are available also from publications summarizing the impact and technique of cTCD for diagnosis of PFO [29,30].

cTCD uses air-containing echo contrast agents (CAs) which normally are unable to pass the pulmonary capillary bed. The diagnosis of a RLS by cTCD is established if TCD observes microembolic signals after contrast injection. However, the minimal amount of microembolic signals suggestive of a clinically relevant RLS is not established [16]. Different authors require different numbers of microembolic signals for the diagnosis of a PFO. They range from a minimum of one microembolus to more than five microemboli. In addition, the time from contrast injection to signal detection ranges from 6 to 10 cardiac cycles or from 4 s to 24 s [31—33]. Most authors used agitated saline solution as contrast agent [4,18,33—39] or D-galactose Mb solution (Echovist®) [12,32,34,40—46]. Only few authors used other agents such as Oxypolygelatine (Gelifundol®, Gelofusin®) [3,31,39]. A sensitivity up to 100% was achieved by both Echovist® [42,47] and agitated saline solution [4,35,38]. The Consensus Meeting recommended using the saline/air mixture. Saline/air mixture is not subject to local approval rules and has proven as effective as Echovist® in numerous studies. However, Echovist® is out of use in most countries because this CA is not longer commercially available.

Recommendations

In younger stroke patients, studies that can identify PFO or ASA may be considered for prognostic purposes (class II, level C). Echocardiography is recommended in selected stroke and TIA patients, and particularly in cryptogenic stroke and when paradoxical embolism is suspected (class III, level B). TCD is probably useful to detect cerebral microembolic signals in a wide variety of cardio- and cerebrovascular disorders or procedures (classes II—IV, level B). Standardized technique cTCD has a sensitivity similar to cTEE for detection of a PFO with RLS (class II, level A) but does not provide information of the anatomic location of the shunt or the presence of an ASA. The examination should be performed according to the instructions of the International Consensus Conference [16] (class II, level A). Although cTCD provides information about the size of the shunt, the clinical usefulness remains to be determined (level C). cTEE remains the ''golden standard'' for the detection of PFO. However, cTCD can be used as a minimally invasive screening test before cTEE or as an alternative method if cTEE is not available (classes III—IV, level C).

Uncertainties exist regarding optimal treatment of paradoxical cerebral embolism and therapeutic considerations have focussed primarily on the management of